

FIG. 1

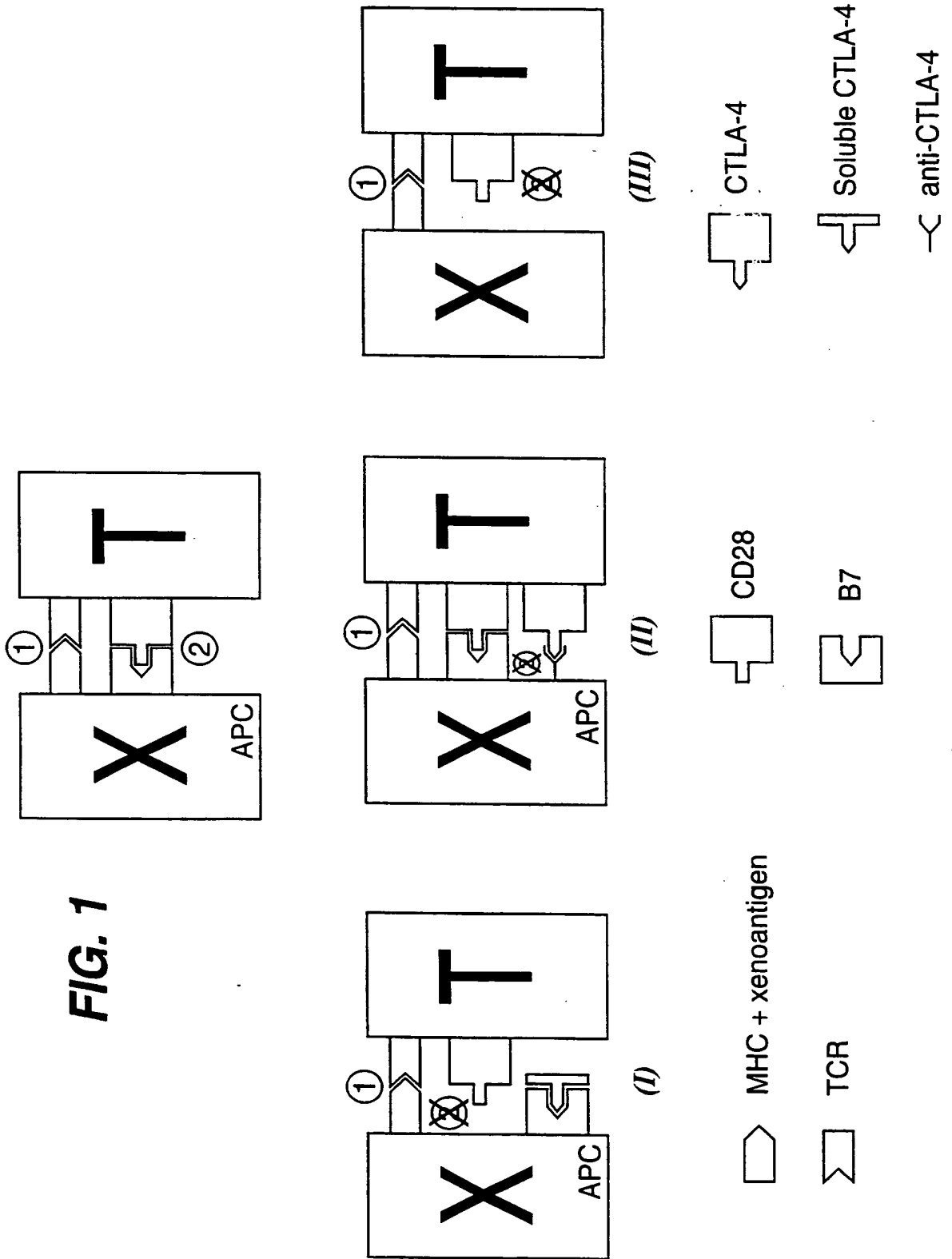


FIG. 2

-30	-20	-10	1	11	21
MACSGFRSHG	AWLETSRTW	PCTALFSLLF	IPVFSKGMHV	AQPAVVLANS	RGVASFVCEY
••L•QR•K	•Q•N•AA••	••L•F•••	•••C•A•••	••••••S•	••I••••••
••••Q•••	T•W-•••••	•••••F•V•	••••••N•	T••P•••S•	•••••S••
			*		
31	41	51	61	71	81
GSAGKAAEVR	VTVLRAGSQ	MTEVCAATYT	VEDELTFLDD	STCTGTSTEN	KVNLTIQGLR
A•P•••T••	••••Q•D••	V•••••M	MGN•••••	•I••••SG•	Q•••••••
E•S•••D••	••••E•••	V••••G•M	•••••••	••I•••RG•	••••••••
91	101	111	121	131	141
AVDTGLYICK	VELLYPPPY	VGMNGTQIY	VIDPEPCPDS	DFLLWILAAV	SSGLFFYSFL
•M•••••	••MYPPPY	L•I•••A••	•••••••	•••••••	•••••••
•M••••V••	••MYPPPY	•I•••••	•••••••	•••••••	•••••••
			*		
151	161	171	181	SEQ ID:1 (pCTLA4)	
ITAVSLSKML	KKRSPLTTGV	YVKMPPTPE	CEKQFQPYFI	PIN	
L••••••	•••••••	•••••••	•••••••	•••	
•••••••	•••••••	•••••••	•••••••	Human CTLA4	
				Cattle CTLA4	

FIG. 3

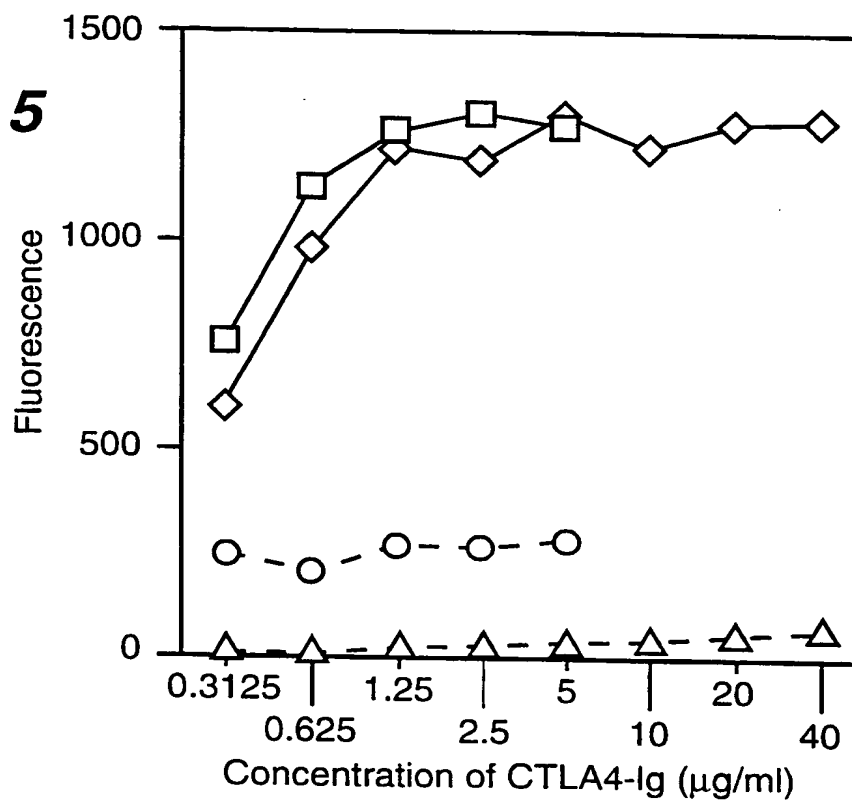
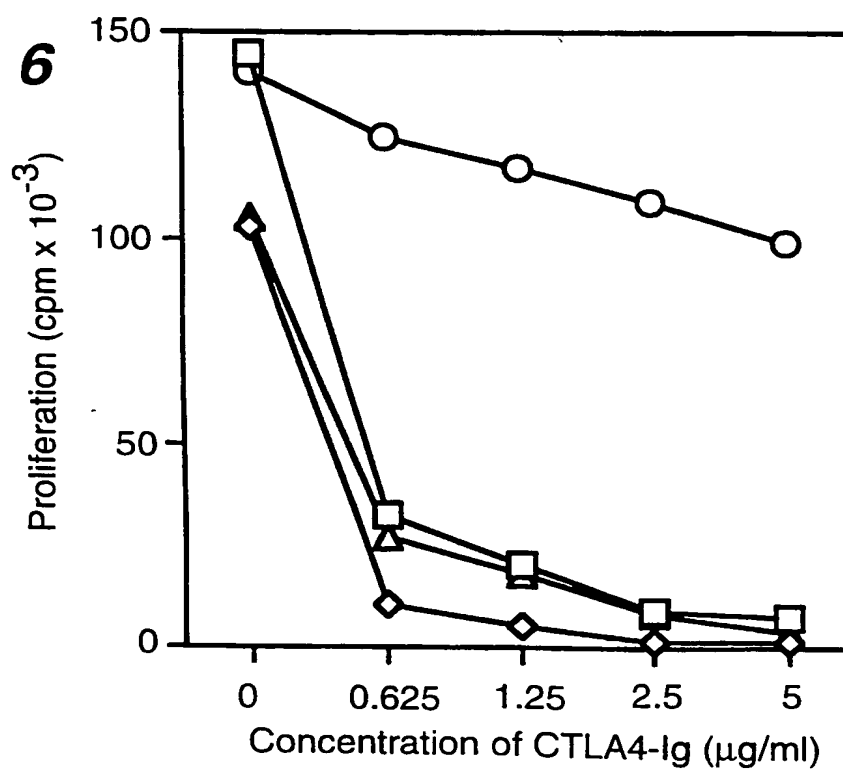
1	11	21	31	41	51
ATGGCTTGCT	CTGGATTCCG	GAGCCATGGG	GCTTGGCTGG	AGCTTACTTC	TAGGACCTGG
.....C	T.....T.A	C.G.CAA	..CA...A	C.GG.G	C.....
.....A	..T.....	A.....	-----A
61	71	81	91	101	111
CCCTGTACAG	CTCTGTTTC	TCTTCTCTTC	ATCCCTGTCT	TCTCCAAAGG	GATGCACGTG
.....C	TC.....TG.....C	A.....
.....C.T	C..A...T	..G.....T	..T.....	..A.T..
121	131	141	151	161	171
GCCCAACCTG	CAGTAGTGCT	GGCCAACAGC	CGGGGTGTG	CCAGCTTGT	GTGTGAGTAT
.....G...	T..G..A..G...	..A..CA..
A.....G..CG.....	..T.G....CTC	A.....A..
181	191	201	211	221	231
GGGTCTGCAG	GCAAAGCTGC	CGAGGTCCGG	GTGACAGTGC	TGCGGCGGGC	CGGCAGCCAG
..CA...C...CA..	T.....	T.....A..	T.A.....
A.....T...AGA..	A.....
241	251	261	271	281	291
ATGACTGAAG	TCTGTGCCGC	GACATATACT	GTGGAGGATG	AGTTGACCTT	CCTTGATGAC
G.....G..	A..C..C..TG	A..G..A..A.....T
G.....C...TG	..C..C..TGC.A.....	..G.....T
301	311	321	331	341	351
TCTACATGCA	CTGGCACCTC	CACCGAAAAC	AAAGTGAACC	TCACCATCCA	AGGGCTGAGA
..C..TC...	..G.....	..GT..G...T	C.....	..T.....	..A.....G

SEQ ID: 2 (pCTLA4)
Human CTLA4
Cattle CTLA4

FIG. 3 (CONTD.)

-30	-20	-10	1	11	21
MACSGFRSHG	AWLELTSRTW	PCTALFSLLF	IPVFSKGMHV	AQPAVVLANS	RGVASFVCEY
31	41	51	61	71	81
GSAGKAAEVR	VTVLRRAQSQ	MTEVCAATYT	VEDELTFLDD	STCTGTSTEN	KVNLTIQGLR
91	101	111	121	131	141
AVDTGLYICK	VELLYPPPY	VGMNGTQIY	VIDPEPCDS	DGSGGAAEP	KSCDKTHTCP
151	161	171	181	191	201
PCPAPELLGG	PSVFLFPPKP	KDTLMIS RTP	EVTCVVVDVS	HEDPEVKFNW	YVDGVEVHNA
211	221	231	241	251	261
KTKPREEQYN	STYRVVSVLT	VLHQDWLNGK	EYCKKVS NKA	LPAPIEKTIS	KAKGQPREPQ
271	281	291	301	311	321
VYTLPPSRDE	LTKNQVSLTC	LVKGFYPSDI	AVEWESNGQP	ENNYKTT PPV	LDSDGSFFLY
331	341	351	361		
SKLTVDKSRW	QQGNVFSCSV	MHEALHNHYT	QKSLSLSPGK		

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FIG. 5**FIG. 6**

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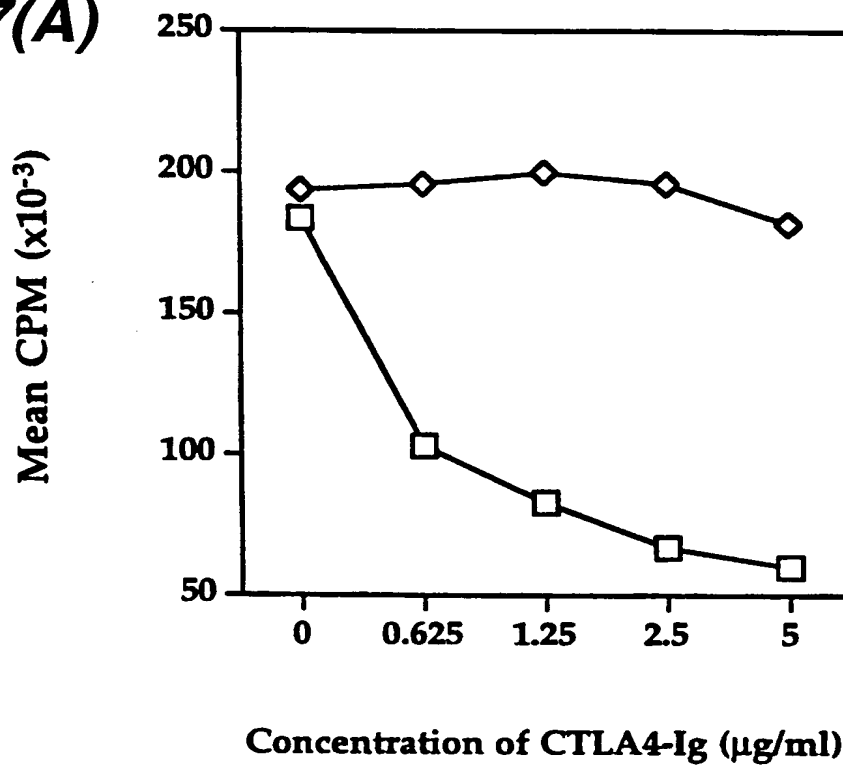
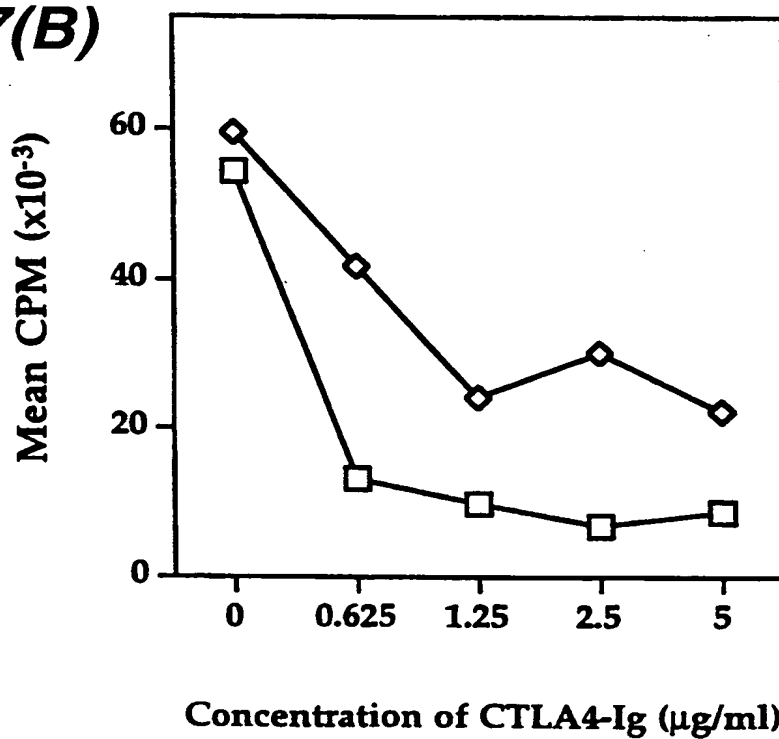
FIG. 7(A)**FIG. 7(B)**

FIG. 8

1..... 11..... 21..... 31..... 41..... 51..... 61..... 71.....
 CCGAGGTGCA GCTGGTGGAG TCTGGGGGAG GCTTGGTACA GCCTGGGGGG TCCCTGAGAC TCTCCTGTGC AGCCTCTGGA
 81..... 91..... 101..... 111..... 121..... 131..... 141..... 151.....
 TTCACCTTA GCAGCTATGC CATGAGCTGG GTCCGCCCAGG CTCCAGGGAA GGGGCTGGAG TGGGTCTCAG CTATTAGTGG
 161..... 171..... 181..... 191..... 201..... 211..... 221..... 231.....
 TAGTGGTGGT AGCACATACT ACGCAGACTC CGTGAAGGC CGGTTCAACA TCTCCAGAGA CAATTCCAAG AACACGCTGT
 241..... 251..... 261..... 271..... 281..... 291..... 301..... 311.....
 ATCTGCAAAT GAACAGCCTG AGAGCCGAGG ACACGGCCGT GTATTACTGT GCAAGAGCTG GTCGTATTT GTTTGACTAT
 321..... 331..... 341..... 351..... 361..... 371..... 381..... 391.....
 TGGGGCCCAAG GTACCCTGGT CACCGTCTCG AGTGGTGGAG GCGGTTTCAGG CGGAGGTGGC TCTGGCGGTA GTGCACCTCA
 401..... 411..... 421..... 431..... 441..... 451..... 461..... 471.....
 GTCTGTGCTG ACTCAGCCAC CCTCAGCGTC TGGGACCCCC GGCAGAGGG TCACCATCTC TTGTTCTGGA AGCAGCTCCA
 481..... 491..... 501..... 511..... 521..... 531..... 541..... 551.....
 ACATCGGAAG TAATTATGTA TACTGGTACC AGCAGCTCCC AGGAACGGCC CCCAACTCC TCATCTATAG GAATAATCAG
 561..... 571..... 581..... 591..... 601..... 611..... 621..... 631.....
 CGGCCCTCAG GGGTCCCTGA CCGATTCTCT GGCTCCAAGT CTGGCACCTC AGCCTCCCTG GCCATCAGTG GGCTCCGGTC
 641..... 651..... 661..... 671..... 681..... 691..... 701..... 711.....
 CGAGGATGAG GCTGATTATT ACTGTGCAGC ATGGGATGAC AGCCTGGTAT TCGGCGGAGG GACCAAGCTG ACCGTCCTAG

721
GT

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FIG. 9

1..... 11..... 21..... 31..... 41..... 51..... 61..... 71.....
 EVQLVESGGG LVQPGGSLRL SCAASGFTFS SYAMSWVRQA PGKGLEWVSA ISGSGGSTYY ADSVKGRFTI SRDNSKNTLY

 81..... 91..... 101..... 111..... 121..... 131..... 141..... 151.....
 LQMSLRAED TAVYYCARAG RILEDYWGQG TLTVVSSGGG GSGGGSGGS ALQSVLTQPP SASGTPGQRV TISCSGSSSN
 LINKER

 161..... 171..... 181..... 191..... 201..... 211..... 221..... 231.....
 IGSNYVYVYQ QLPGTAPKLL IYRNNQRPSSG VPDRFSGSKS GTSASLAISG LRSEDEADYY CAWDDSLVF GGTGKLTVLG

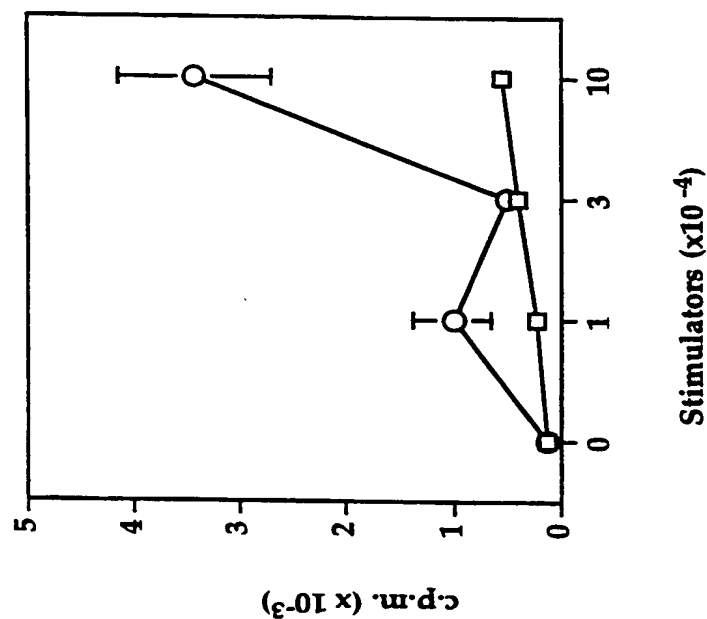


FIG. 13

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FIG. 10

	10	20	30	40	50	60	
M1 sFv	CATGG-CCGAGGTGCAGCTGGTGGAGTCTGGGGGAGGCTTGGTACAGCCTGGGGGGTCCCTGAG						
M3 sFv	CATGG-CCCAGGTGCAGCTGCAGGAGTCCGGGCCAGGACTGGTGAAGCCTTCGGAGACCTGTGC						
M19 sFv	CATGG-CCCAGGTGCAGCTGGTGCAGTCTGGGGCTGAGGTGAAGAGGCCTGGGGCCTCAGTGAA						
M24 sFv	CATGGGGCCAGGTGCAGCTGTTGCAGTCTGCAGCAGAGGTGAAAAAGCCCCGGGAGTCTCTGAA						
	70	80	90	100	110	120	
M1 sFv	ACTCTCCTGTGCAGCCTCTGGATTACCTTTAGCAGC--TA--TGCCAT--GAGCTGGGTCCGC						
M3 sFv	CCTCACCTGCAGTGTCTCTGGTGGCTCCGTGCAGCAGTGGTAGTTACTACTGGAGCTGGATCCGG						
M19 sFv	GGTTTCCTGCAAGGCATCTGGATACACCTTCACCAGC-----TACTATATGCACTGGGTGCGA						
M24 sFv	GATCTCCTGTAAGGGTTCTGGATACAGCTTTACCAGC-----TACTGGATCGGCTGGGTGCGC						
	130	140	150	160	170	180	190
M1 sFv	CAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGGTAGTGGTGGTAGCACATACT						
M3 sFv	CAGCCCCCAGGGAAGGGACTGGAGTGGATT--GGGTAT-ATCTATTACAGTGGGAGCACCAACT						
M19 sFv	CAGGCCCCCTGGACAAGGGCTTGAGTGGATGGGAATAATCAACCCCTAGTGGTGGTAGCACAAGCT						
M24 sFv	CAGATGCCCGGAAAGGCCCTGGAGTGGATGGGGATCATCTATCCTGGTGACTCTGATACCAGAT						
	200	210	220	230	240	250	
M1 sFv	ACGCAGACTCCGTGAAGGGCCGGTTACCATCTCCAGAGACAATTCCAAGAACAGCTGTATCT						
M3 sFv	ACAACCCCTCCCTCAAGAGTCGAGTCACCATATCAGTAGACACGTCCAAGAACCAGTTCTCCCT						
M19 sFv	ACGCACAGAAGTTCAGGGCAGAGTCACCATGACCAGGGACACGTCCACGAGCACAGTCTACAT						
M24 sFv	ACAGCCCGTCCCTCCAAGGCCAGGTACCATCTCAGCCGACAAGTCCATCAGCACCCGCTACCT						
	260	270	280	290	300	310	320
M1 sFv	GCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTGTATTACTGTGCAAGAGCTG-----GT						
M3 sFv	GAAGCTGAGCTCTGTGACCGCTGCGGACACGGCCGTGTATTACTGTGCAAGAATGC-----GG						
M19 sFv	GGAGCTGAGCAGCCTGAGATCTGAGGACACGGCCGTGTATTACTGTGCAAGAGTGGCTCCCTAT						
M24 sFv	GCAGTGGAGCAGCCTGAAGGCCTCGGACACGGCCGTGTATTACTGTGCAAGATT--TTGCT-T						
	330	340	350	360	370	380	
M1 sFv	CGTATTTTGTTTGACTATTGGGGCCAAGGTACCCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						
M3 sFv	AAGGATAAGTTTGTGACTATTGGGGCCAAGGTACCCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						
M19 sFv	GTGAATACGCTTGTTTGGGGCCAAGGTACCCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						
M24 sFv	GGTGGT---TTTGTGACTATTGGGGCCAAGGTACCCCTGGTCACCGTCTCGAGTGGTGGAGGCGGTT						

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390 400 410 420 430 440

M1 sFv CAGGCGGAGGTGGCTCTGGCGGTAGTGCACTTCAGTCTGTGCTGACTCAG---CCACCCCTCAGC
M3 sFv CAGGCGGAGGTGGCTCTGGCGGTAGTGCACTTCAGTCTGTGCTGACTCAG---CCACCCCTCAGC
M19 sFv CAGGCGGAGGTGGCTCTGGCGGTAGTGCACTTTCCTCTGAGCTGACTCAG---GACCCCTGCTGT
M24 sFv CAGGCGGAGGTGGCTCTGGCGGTAGTGCACTTGACATCCAGTTGACCCAGTCTCCATCCTTCCT

450 460 470 480 490 500 510

M1 sFv GTCTGGGACCCCGGGCAGAGGGTCACCATCTCTTGTCTGGAAGCAGCTCCAACATCGGAAGT
M3 sFv GTCTGGGACCCCGGGCAGAGGGTCACCATCTCTTGTCTGGAAGCAGCTCCAACATCGGAAGT
M19 sFv GTCTGTGGCCTTGGGACAGACAGTCAGGATCACATGCCAAGGAGACAGCCTCA-----GAAGC
M24 sFv GTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCC---GGCCAGTCAGGGCATT---AGC

520 530 540 550 560 570

M1 sFv AATTATGTATACTGGTACCAGCAGCTCCAGGAACGGCCCCCAAACCTCCTCATCTATAGGAATA
M3 sFv AATTATGTATACTGGTACCAGCAGCTCCAGGAACGGCCCCCAAACCTCCTCATCTATAGGAATA
M19 sFv TATTATGCAAGCTGGTACCAGCAGAAGCCAGGACAGGCCCCCTGTACTTGTCTATCTATGGTAAAA
M24 sFv AGTTATTTAGCCTGGTATCAGCAAAAACCAGGGAAGCCCCCTAAGCTCCTGGTCTATGCTGCAT

580 590 600 610 620 630 640

M1 sFv ATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCT
M3 sFv ATCAGCGGCCCTCAGGGGTCCCTGACCGATTCTCTGGCTCCAAGTCTGGCACCTCAGCCTCCCT
M19 sFv ACAACCGGCCCTCAGGGATCCAGACCGATTCTCTGGCTCCAGCTCAGGAAACACAGCTTCCTT
M24 sFv CCACCTTGCAAAGTGGGGTCCCATCAAGGTTCAAGGCGCAGTGATCTGGGACAGAATTCACTCT

650 660 670 680 690 700

M1 sFv GGCCATCAGTGGGCTCCGGTCCGAGGATGAGGCTGATTATTACTGTGCAGCATGGGATGACAGC
M3 sFv GGCCATCAGTGGGCTCCGGTCCGAGGATGAGGCTGATTATTACTGTGCAGCATGGGATGACAGC
M19 sFv GACCATCACTGGGGCTCAGGCGGAAGATGAGGCTGACTATTACTGTAACCTCCCGGACAGCAGT
M24 sFv CACAATCAGCAGCCTGCAGCCTGAAGATTTTGCAACTTATTACTGTCA---ACAGCTTAATAGT

710 720 730 740 750

M1 sFv ---CTG---GTATTTCGGCGGAGGGACCAAGCTGACCGTCCCTAGGTGC
M3 sFv ---CTGT---TTGTATTTCGGCGGAGGGACCAAGCTGACCGTCCCTAGGTGCGGCGGC
M19 sFv GGTTTACTGTATTTCGGCGGAGGGACCAAGCTGACCGTCCCTAGGTGC
M24 sFv TACCGCTTGACGTTTCGGCCAAGGGACCAAGCTGGAAATC---AAACGTG---C

FIG. 10 (CONTD.)

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FIG. 11

	10	20	30	40	50	60
M1 sFv Peptide
M3 sFv Peptide	MAQVQLQESGPGLVKPS	ETLSLTCTVSGGSVSSGS	YWSWIRQPPGKLEWIG	ITY-YSG		
M19 sFv Peptide	--QVQLVQSGAEVKRFG	ASVKVSCKASG--YTFT	SYMHWIRQAPGQGLEW	MGIINPSG		
M24 sFv peptide	--QVQLVQSAAEVKKPG	ESLKISCKGSG--YSFT	SYWIGWIRQMPGKLEW	MGLIYPGDS		
	70	80	90	100	110	120
M1 sFv Peptide
M3 sFv Peptide	STYYADSVKGRFTISRD	NSKNITLYQMNSLRAED	TAVYYCARAGR--ILFD	YWGQGITLVT		
M19 sFv Peptide	STINYNPSLKSRTVIS	VDTSKNQFSLKLSVTA	ADTAVYYCARMRK--DK	FDYWGQGITLVT		
M24 sFv peptide	STSYAQKFQGRVTIMR	DTSTSTVYMESSLRSE	DTAVYYCARVAFVNTL	VFYWGQGITLVT		
	130	140	150	160	170	180
M1 sFv Peptide
M3 sFv Peptide	VSSGGGGSGGGSGGS	ALQSVLTQPPS-ASGT	PGQRTVITSCSGSSN	IGSNVYVWYQQLP		
M19 sFv Peptide	VSSGGGGSGGGSGGS	ALQSVLTQPPS-ASGT	PGQRTVITSCSGSSN	IGSNVYVWYQQLP		
M24 sFv peptide	VSSGGGGSGGGSGGS	ALSSSLTQDPA-VS	VALGQTVRTICQGD	S--LRSYASWYQQKP		
	190	200	210	220	230	240
M1 sFv Peptide
M3 sFv Peptide	GTAPKLLIYRNQRP	SGVPRDFSGSKSGT	SASLAI	SGLRSEDEADY	YCAWDDSLF-VFG	
M19 sFv Peptide	GTAPKLLIYRNQRP	SGVPRDFSGSKSGT	SASLAI	SGLRSEDEADY	YCAWDDSLF-VFG	
M24 sFv peptide	GQAPVLVIYGNRPS	GIPDRFSGSSGN	IASLITTTGAQAE	DEADYCN	SRDSSGFTVFG	
	...					
M1 sFv Peptide	GGIKLIVLG					
M3 sFv Peptide	GGIKLIVLGAA					
M19 sFv Peptide	GGIKLIVLG					
M24 sFv peptide	QGIKLEI--KR					

FIG. 12

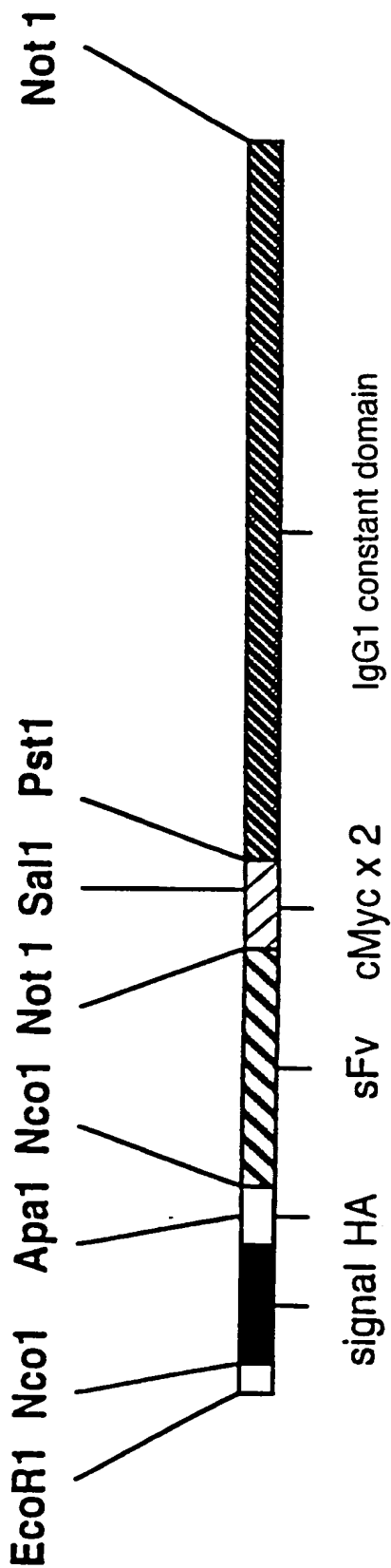
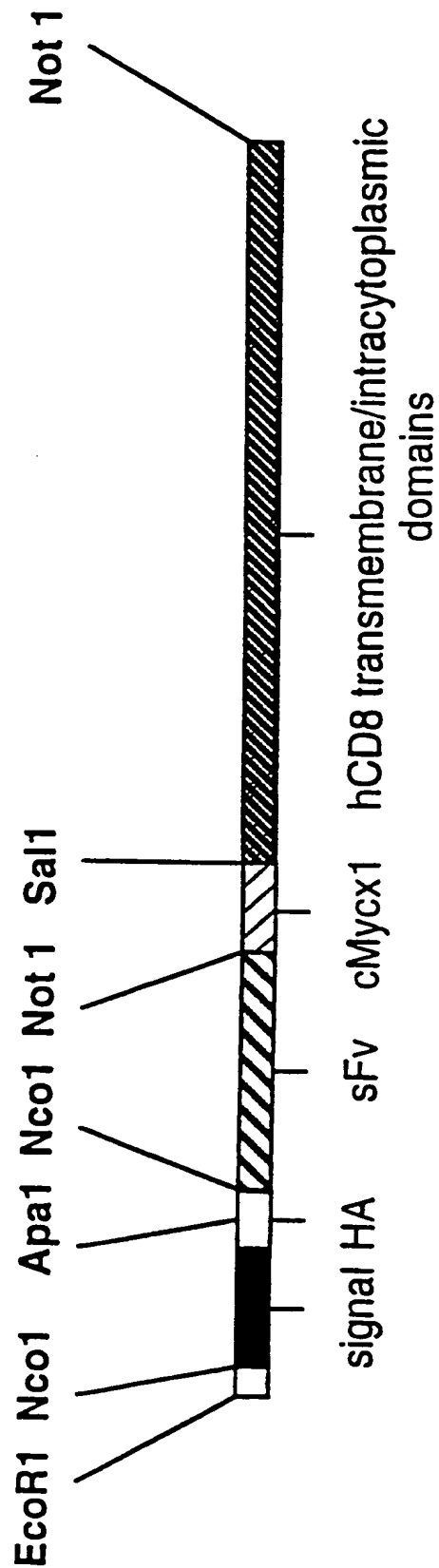


FIG. 14



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FIG. 15(A)

-65 AGCTTCAGGA TCCTGAAAGG TTTTGCTCTA CTTCTGAAG ACCTGAACAC
-15 CGCTCCCAT AAGCCATGGC TTGCCTTGGA TTTCAGCGGC ACAAGGCTCA
36 GCTGAACCTG GCTACCAGGA CCTGGCCCTG CACTCTCCTG TTTTTTCTTC
86 TCTTCATCCC TGTCTTCTGC AAAGCAATGC ACGTGGCCCA GCCTGCTGTG
136 GTACTGGCCA GCAGCCGAGG CATCGCCAGC TTTGTGTGTG AGTATGCATC
186 TCCAGGCAAA GCCACTGAGG TCCGGGTGAC AGTGCTTCGG CAGGCTGACA
236 GCCAGGTGAC TGAAGTCTGT GCGGCAACCT ACATGATGGG GAATGAGTTG
286 ACCTTCCTAG ATGATTCCAT CTGCACGGGC ACCTCCAGTG GAAATCAAGT
336 GAACCTCACT ATCCAAGGAC TGAGGGCCAT GGACACGGGA CTCTACATCT
386 GCAAGGTGGA GCTCATGTAC CCACCGCCAT ACTACCTGGG CATAGGCAAC
436 GGAACCCAGA TTTATGTAAT TGATCCAGAA CCGTGCCCAG ATTCTGACTT
486 CCTCCTCTGG ATCCTTGACAG CAGTTAGTTC GGGGTGTGTT TTTTATAGCT
536 TTCTCCTCAC AGCTGTTTCT TTGAGCAAAA TGCTAAAGAA AAGAAGCCCT
586 CTTACAACAG GGGTCTATGT GAAAATGCCC CCAACAGAGC CAGAATGTGA
636 AAAGCAATT CAGCCTTATT TTATTCCCAT CAATTGAGAA TT

FIG. 15(B)

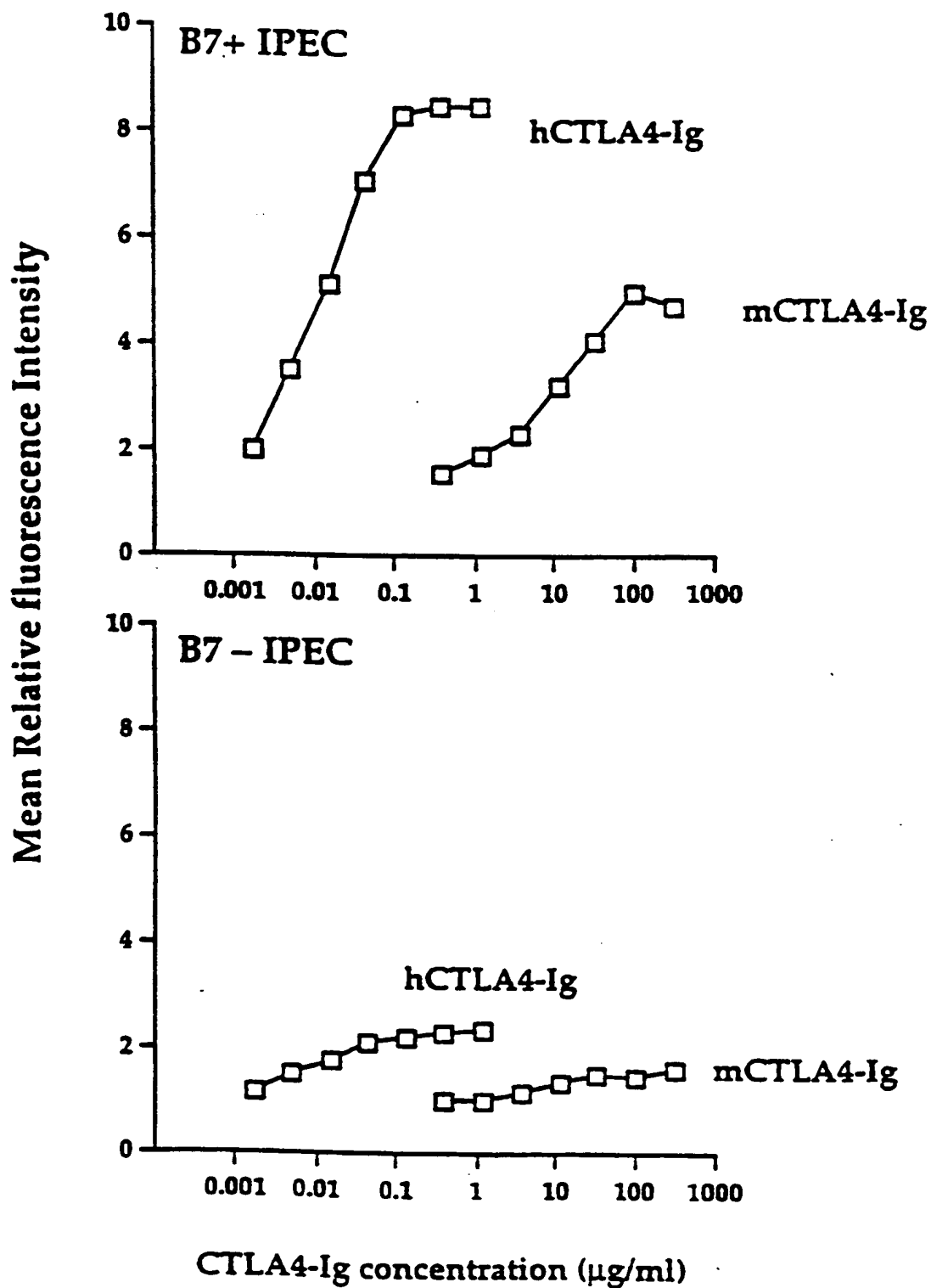
-30 -20 -10 1 11 21
MACLGFORHK AQLNLATRTW PCTLLFLLF IPVECKAMHV AQPAVVLASS RGIASFVCEY
★
31 41 51 61 71 81
ASPGKATEVR VTVLRQADSQ VTEVCAATYM MGNELTFLDD SICTGTSSGN QVNLTIQGLR
91 101 111 121 131 141
AMDTGLYICK VELMYPPPY LGIGNGTQIY VIDPEPCPDS DFLWILA AV SSGLEFFYSFL
★
151 161 171 181
LTAVSLSKML KKRSPLETTGV YVKMPPEPE CEKQFQPYFI PIN
★

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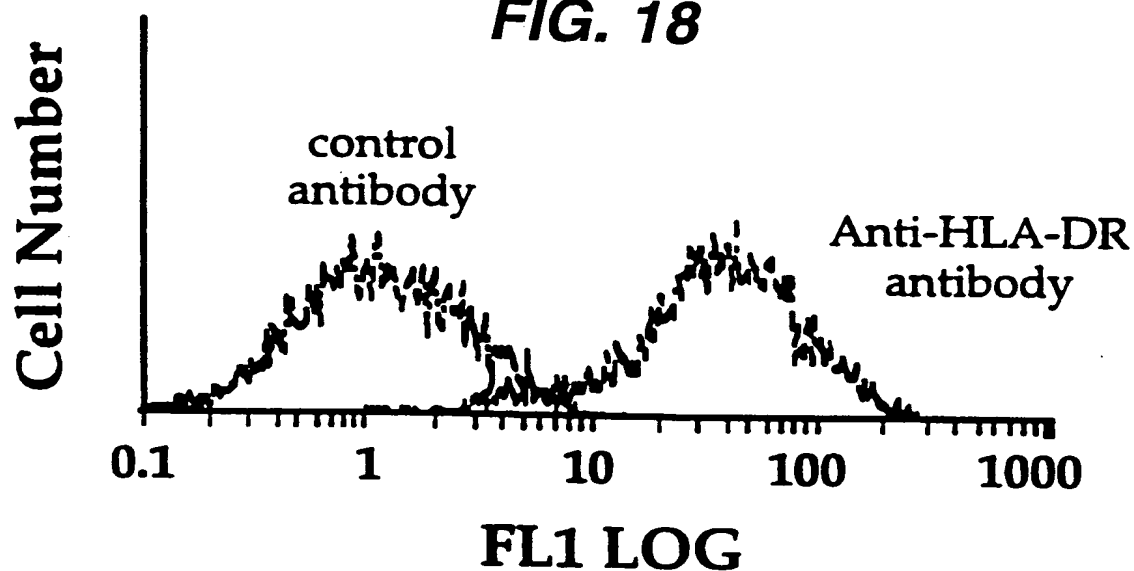
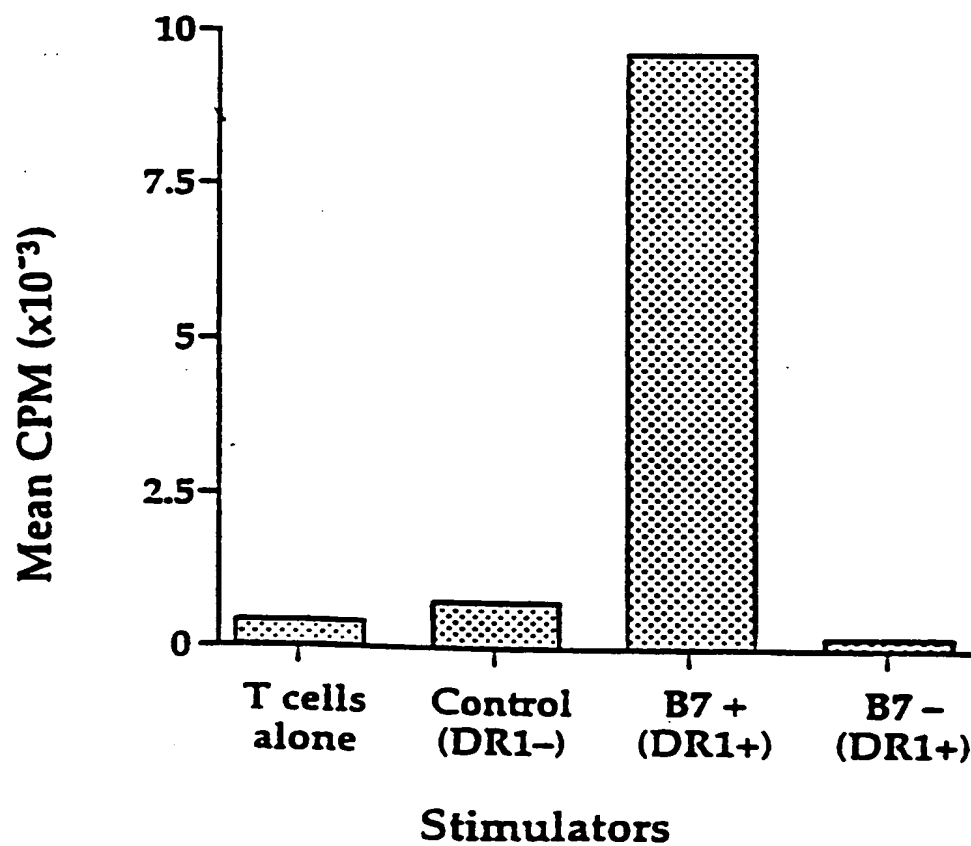
FIG. 16

-36 AAGCTTCGAG CCAAGCAGCG TCCTGGGGAG CGCGTCATGG CCTTACCAGT
15 GACCGCCTTG CTCCTGCCGC TGGCCTTGCT GCTCCACGCC GCCAGGCCGA
65 GCCAGTTC CG GGTGTCGCCG CTGGATCGGA CCTGGAACCT GGGCGAGACA
115 GTGGAGCTGA AGTGCCAGGT GCTGCTGTCC AACCCGACGT CGGGCTGCTC
165 GTGGCTCTTC CAGCCGCGCG GCGCCGCCGC CAGTCCCACC TTCCTCCTAT
215 ACCTCTCCCA AAACAATCCC AAGGCGGCCA AGGGGCTGGA CACCCAGCGG
265 TTCTCGGGCA AGAGGTTGGG GGACACCTTC GTCCTCACCC TGAGCGACTT
315 CCGCCGAGAG AACGAGGGCT ACTATTTCTG CTCGGCCCTG AGCAACTCCA
365 TCATGTACTT CAGCCACTTC GTGCCGGTCT TCCTGCCAGC GAAGCCCACC
415 ACGACGCCAG CGCCGCGACC ACTAACACCG GCGCCCACCA TCGCGTCGCA
465 GCCCCTGTCC CTGCGCCCAG AGGCGTGCCG GCCAGCGGCG GGGGGCGCAG
515 TGCACACGAG GGGGCTGGAC TTCGCCTGTG ATATCTACAT CTGGGCGCCC
565 CTGGCCGGGA CTTGTGGGGT CCTTCTCCTG TCACTGGTTA TCACCCTTTA
615 CTGCAACCAC AGGAACCGAA GACGTGTTTG CAAATGTCCC CGGCCTGTGG
665 TCAAATCGGG AGACAAGCCC AGCCTTTCGG CGAGATACGT CTAACCCTGT
715 GCAACAGCCA CTACATGAAT TCC

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FIG. 17

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FIG. 18**FIG. 19**

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FIG. 20

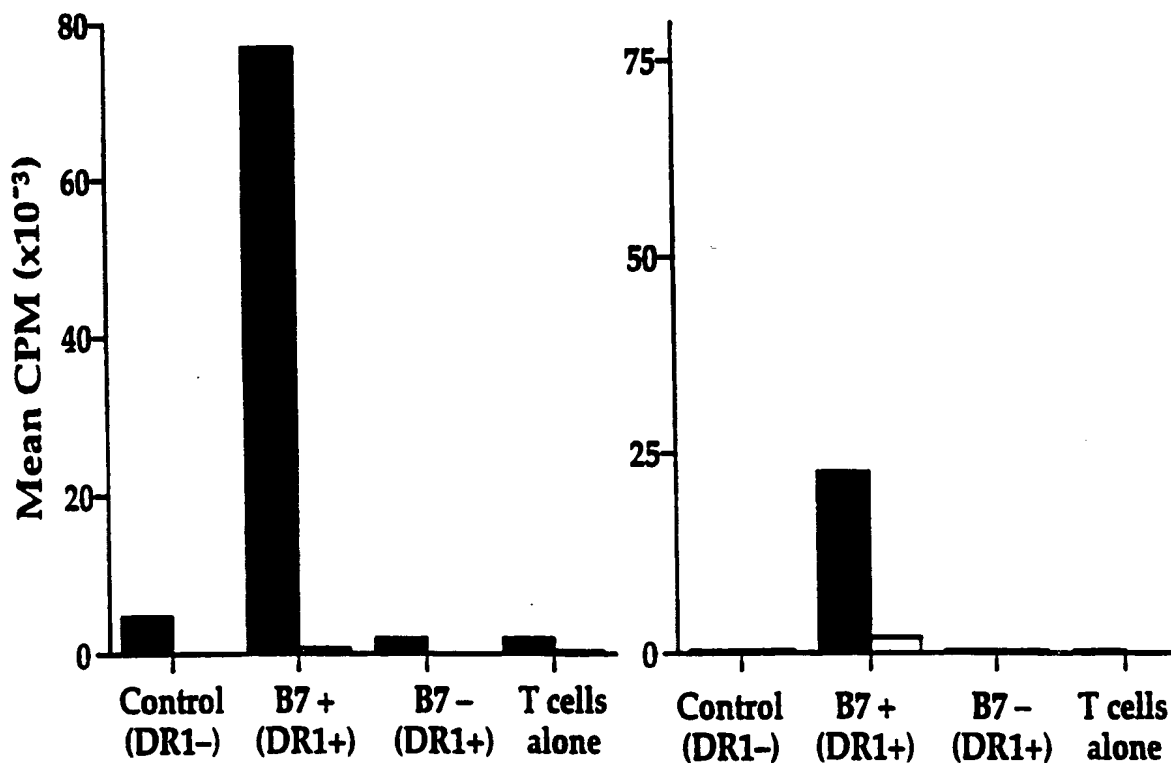


FIG. 21

